REMARKS

The claims have been amended to clarify the nature of the invention and to obviate the rejection for indefiniteness. The term "macrolide," which the Office considers ambiguous, has been replaced by "macrolactone polyketide" which clarifies that the substrate in the preparation of an antibiotic is the end-product of the polyketide synthase gene cluster. The further tailoring reactions to confer antibiotic activity are thus carried out in *S. erythraea*. In addition, it has been clarified that the macrolactone polyketide must be heterologous to the *S. erythraea*; and produced recombinantly; thus, as well as other than 6-dEB. No new matter has been added and entry of the amendment is respectfully requested. Support for the insertion of "heterologous and recombinantly produced" to claim 19 is supported by Example 4 which describes this process as performed on heterologous and recombinantly produced polyketides.

Formal Matters

The position taken by the Office on priority is noted; however, this issue is moot as there are no intervening publications. The specification has been updated as requested; the title has been changed and a new abstract is supplied. Reference is made to Figure 3 in claim 24 as requested.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 19-24 were rejected under this statutory section because of the apparent confusion between with term "macrolide" and "antibiotic." The requested clarification has been added to the claims by replacing "macrolide" with "macrolactone polyketide," thus clarifying that the functions performed by *S. erythraea* are tailoring functions that operate on the products of polyketide synthase cluster.

The full name of 6-dEB is now included in the claims.

It is believed that these amendments address all grounds for rejection on this basis.

The Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 20 was rejected under this section as putatively lacking written description citing *Regents of the University of California v. Eli Lilly*, 119 F3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). It is believed that in the context of the present claims, this citation is inapposite. The claims in the *Lilly* case were directed to specific nucleic acid molecules the nature of which could not be ascertained without a complete description of their structure. Here, however, the claims are directed to a method where the exact structure of *S. erythraea* used to conduct the method is irrelevant. All that is required is that it be rendered functionally unable to produce a macrolide. Means to destroy the capability to prepare its normal products by, random mutation techniques for example, are well known in the art. It would clearly not take undue experimentation to produce a mutant of *S. erythraea* that does not produce a macrolactone polyketide. There is no showing made by the Office that one of ordinary skill would be unable to obtain such a mutant without undue experimentation. The claim is not directed to a particular mutant itself, but rather to a process which can use any mutant which does not itself make a macrolactone polyketide. The ease of obtaining such mutants is, indeed, illustrated by the Weber, *et al.*, article cited by the Office. Thus, the subject matter of claim 20 is adequately described, and this rejection may properly be withdrawn.

Also rejected under this section were claims 21-24. Claim 22 has been canceled and claims 23-24 now depend on claim 20 and are thus addressed in the above discussion.

Claim 21 is thus now the only pertinent claim.

With respect to this claim, applicants do not agree that the Weber article fails to teach a method to make such mutants. A34 refers to only a chromosomal marker and the article

describes how to obtain mutants and screen for such markers. Accordingly, it is respectfully submitted that no deposits should be required.

The Rejections Under 35 U.S.C. § 102(e)

Claims 19 and 20 were rejected as assertedly anticipated by Katz, *et al.*: Claims 21-24 were free of this rejection. However, as claims 23 and 24 now depend from claim 20, it is believed that the Office may consider claim 23 to be subject to this rejection; claim 24 is clearly free of Katz as the specific compounds fed to the *S. erythraea* do not appear in Katz. Claims 19-20 and 23 are free of this rejection as well. The claims require adding a heterologous and recombinantly produced macrolactone polyketide to the culture medium of *S. erythraea*. As correctly described by the Office, Katz does not disclose this process. The *S. erythraea* is instead fed a butyl thioester of a δ-lactone; this is not a macrolactone polyketide. Accordingly, this basis for rejection may also be withdrawn.

CONCLUSION

The claims have been amended to accommodate formal rejections, and have been shown to meet the written description requirements. The reason Katz fails to anticipate the claims has been explained. Accordingly, applicants respectfully request that claims 19-21 and 23-24 be passed to issue.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 300622000212.

Respectfully submitted,

Dated: April 3, 2003

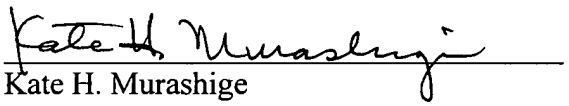
By: 

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please amend the paragraph on page 1, lines 4-7, after "CROSS REFERENCE TO RELATED APPLICATIONS" as follows:

This application is [A] a divisional of US Serial No. 09/434,289 now U.S. patent 6,261,816, which is a continuation of U.S. Serial No. 08/896,323, filed 17 July 1997 and now U.S. Patent 6,066,721 which is a continuation-in-part of US Serial No. 08/675,817 filed 5 July 1996 now U.S. Patent 6,080,555, which claims priority under 35 USC 119(e)(1) from provisional application serial number 60/003,338 filed 6 July 1995. The contents of these applications are incorporated herein by reference.

In the Claims:

19. (Amended) A method to prepare an antibiotic which method comprises adding a [macrolide] heterologous and recombinantly produced macrolactone polyketide other than 6-deoxyethronolide B (6-dEB) to the culture medium of *Saccharopolyspora erythraea*;

culturing said *S. erythraea* in said medium so as to convert said [macrolide] macrolactone polyketide into an antibiotic; and

extracting the antibiotic from the medium.

20. (Twice amended) The method of claim 19 wherein the *S. erythraea* is a mutant that itself produces no [macrolide] macrolactone polyketide.

23. (Twice amended) The method of claim [21] 20 wherein said [macrolide] macrolactone polyketide is a 14-member macro[lide] lactone polyketide.

24. (Twice amended) The method of claim 23 wherein said 14-member [macrolide] macrolactone polyketide is 14-propyl 6-dEB (Formula 6 as depicted in Figure 3) or 14-desmethyl-14-phenyl 6-dEB (Formula 7 as depicted in Figure 3).